REMARKS

A. Regarding the Amendments

No claims are amended by the present response. As pending, the claims are supported by the specification and the original claims. Thus, upon entry of the Response, claims 1 and 4-53 will be pending, as set forth in the attached complete "Listing of the Claims."

B. Rejection Under 35 U.S.C. § 102/103

It is not clear to Applicants why the claim rejections section of Paper No. 10 contains the heading "Claim Rejections – 35 USC § 102/103." It does not appear that the action contains any 102 rejections, especially as the language below this heading states "[t]he following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action..." It is therefore assumed that there are no pending 102 rejections of the present application. Clarification is requested if this assumption is incorrect.

Claims 1-53 are rejected under 35 U.S.C. 103(a) as allegedly unpatentable over Evans in view of Tseng, Woodward, Clark, Hoffman, Krall, Almen, EP 0 747 069, Leung, McIntire and Berger. Applicants respectfully traverse the rejection. Initially, it is noted that claims 2 and 3 were cancelled in the Response mailed December 9, 2002. Therefore, the rejection of claims 1-53 will be addressed as applicable to claims 1 and 4-53.

In order for an invention to be obvious, three requirements must be met: 1) there must be some suggestion or motivation to combine the reference teachings; 2) there must be a reasonable expectation of success; and 3) the combined prior art references must teach or suggest all of the claim limitations. It is respectfully submitted that there is no suggestion or motivation to combine Evans with Tseng, Woodward, Clark, Hoffman, Krall, Almen, EP 0 747 069, Leung, McIntire and/or Berger and that there would not have been any expectation of success in any such combination. It is also respectfully submitted that these eleven references taken together do not teach or suggest all of the elements of the claimed invention. It is stated in the present office

action that Applicants' previously presented arguments have been considered, but are deemed unpersuasive in light of the new references McIntire and Berger. Specifically, it is alleged that as McIntire teaches a viscosity modifier of alkyl cyanoacrylates and Berger teaches plasticizing agents, and that with the previously cited references, the collection of eleven cited references teach the claimed invention. Applicants respectfully disagree.

Independent claims 1, 24, 27, 38 and 46 recite a composition or the use thereof. The composition of these claims polymerizes upon contact with an anionic environment and contains two components, where the first component includes at least two polymerizable alkyl cyanoacrylate monomers and the second component includes an oligomer. The second component contains a oligomer of polymerizable alkyl cyanoacrylate monomer, a plasticizer, and an opacifying agent. None of the cited references, alone or in combination teach or suggest such a composition or its use and therefore cannot anticipate the claimed invention.

Evans does not teach or suggest all of the elements of the present invention. While Evans discloses treatment of arteriovenous malformations employing a biocompatible prepolymer, such as a cyanoacrylate, Evans does not teach or suggest use of more than one cyanoacrylate, nor does Evans teach a second component containing a cyanoacrylate oligomer. The claimed invention recites a combination of a first and second component. It is noted that the first component must contain a minimum of at least two polymerizable alkyl cyanoacrylate monomers. Additionally, the plasticizer of the second component serves to render the resulting polymer of the invention flexible (specification, page 16). Such flexibility allows placement of the compositions and inhibition of breakage of the polymer to smaller pieces, that may enter the bloodstream and cause a catastrophic event. In addition to not teaching all of the claim elements, Evans contains no suggestion or motivation to further combine the single cyanoacrylate with another or with a second component, including any of the elements: an oligomer of a polymerizable alkyl cyanoacrylate monomer, a plasticizer, or an opacifying agent. As Evans does not teach or suggest all of the elements of the present invention, nor does it suggest combination of its

teachings with additional elements, it is respectfully submitted that the present invention is not obvious in light of Evans. Evans, even viewed in light of Tseng, Woodward, Clark, Hoffman, Krall, Almen, EP 0 747 069, Leung, McIntire and/or Berger still do not teach or suggest all of the elements of the claimed invention.

Specifically, Tseng discusses 2-cyanoacrylates widely used in surgical fields, however one of skill in the art would not be motivated by the teachings of Tseng to combine these 2-cyanoacrylates with any other cyanoacrylates. Tseng does not teach or suggest the combined use of multiple cyanoacrylates in a composition or addition of a second component comprised of an oligomer of a polymerizable alkyl cyanoacrylate monomer, a plasticizer, and an opacifying agent.

Similarly, while Woodward discloses hexyl 2-cyanoacrylate and evaluates its properties *in vivo*, one of skill in the art would not be motivated by the teachings of Woodward to combine these hexyl 2-cyanoacrylates with any other cyanoacrylates. Woodward does not teach or suggest the combination of the present invention.

Also cited as rendering the claimed invention obvious, when viewed with Evans, Tseung and Woodward are Clark, Krall, Almen, EP 0 747 069 and Leung. Applicants respectfully submit that there is no motivation to combine these references and that the teachings of the cited references do not disclose all of the elements of the claimed invention and therefore the claimed invention is not obvious in light of the references. Specifically, none of Clark, Hoffman, Krall, Almen, EP 0 747 069 and Leung teach or suggest a composition of two components, where the first component contains at least two polymerizable alkyl cyanoacrylates and the second component contains an oligomer of an alkyl cyanoacrylate monomer, a plasticizer and an opacifying agent.

In particular, Clark is cited as discussing that plasticizers give cyanoacrylates flexibility and that stabilizing agents may be added to inhibit polymerization. It is respectfully submitted, however, that these are characteristics well known in the art, as may be seen in the Background

of the Clark reference. As can be seen in col. 2, lines 11 to 39 of Clark, the characteristics of plasticizers and stabilizing agents were well known in the art prior to the filing of Clark. However, even if one of skill in the art used plasticizers or stabilizing agents with cyanoacrylates, the teachings of Clark would not motivate one of skill in the art to combine a plasticizer and stabilizing agent in a two component composition, where the first component contains at least two polymerizable alkyl cyanoacrylates and the second component contains an oligomer of a alkyl cyanoacrylate monomer, a plasticizer and an opacifying agent, such as that in the claimed invention.

Also cited is the Hoffman reference which is alleged to render the present invention obvious, when viewed in light of the other cited references. It is not clear, however, what Hoffman is relied upon to show, as Hoffman, while cited, is not discussed substantively in either the Office Action mailed September 9, 2003 (Paper No. 6) or the Office Action mailed March 26, 2003 (Paper No. 10). It is assumed that Hoffman, like Krall, is cited as teaching a method of female sterilization comprising administration of cyanoacrylates. It is Applicants' position that the claimed invention is not obvious in light of Hoffman, as Hoffman, even when viewed in light of the cited references, does not tech or suggest all elements of the claimed invention. Specifically, Hoffman teaches a method of sterilization utilizing a cyanoacrylate, but in the teachings of Hoffman the cyanoacrylate is administered to induce an inflammatory response and encourage the growth of scar tissue, which results in subsequent blockage of the fallopian tubes. In fact, Hoffman teaches away from the composition of the claimed invention and use of the same, in that use of a composition in the method of Hoffman will degrade after it is administered and has served its function (see col. 1, lines 47-62).

Additionally, Krall is cited as teaching a method of sterilizing females using cyanoacrylates in the fallopian tubes. While Krall describes a composition useful in the formation of a cyanoacrylate plug of the fallopian tubes, Krall in combination with the other cited references does not teach or suggest a combination of two components to form a composition

such as that set forth in the claimed invention. Krall, in combination with any or all of the cited references, does not teach the composition of the claimed invention, which provides a previously undescribed balance of polymerization rate, adhesiveness, biocompatibility and radiopacity.

Similarly, though Almen describes alkyl cyanoacrylates as a good adhesive compromise, and Leung describes alpha cyanoacrylates as good adhesives, neither reference, alone or in combination with the other cited references teaches or suggests the combination of components of the claimed invention. One of skill in the art would not be motivated by the teachings of Almen and/or Leung to develop the claimed combination of two components. While alpha cyanoacrylates are described by Almen and Leung as being good adhesives, there is no teaching or suggestion of utilizing a first component containing at least two polymerizable alkyl cyanoacrylate monomers and a second component containing an oligomer of a polymerizable cyanoacrylate monomer to obtain an optimum composition. Therefore the composition of the claimed invention is not obvious in light of Almen and/or Leung in combination with the other cited references.

Though EP 0747069 describes a medical device for administering compounds like cyanoacrylates, when the teachings of EP 0747069 are taken in combination with the other cited references, it does not teach or suggest administration of the claimed compound, as the combination of references does not teach or suggest the claimed compound itself. Accordingly, the claimed methods of the invention including administration cannot be obvious in light of the combination of EP 0747069 with any or all of the other cited references.

McIntire is cited in Paper No. 10 as teaching that polymers of alkyl cyanoacrylates may be added to monomer alkyl cyanoacrylates as viscosity modifiers and therefore in combination with the teachings of Evans and the other cited references, renders the claimed invention obvious. Applicants respectfully disagree. McIntire teaches a specific method of making poly(α-cyanoacrylates), which may then be used as viscosity modifiers. However, McIntire is not the first to use poly(α-cyanoacrylates) as viscosity modifiers. It is stated in col. 2, lines 34-40 that

the poly(α-cyanoacrylates) prepared by the method of McIntire could be added in smaller amounts than "prior art poly(α-cyanoacrylates)" to achieve the same viscosity effects. Therefore, poly(α-cyanoacrylates) as viscosity modifiers were already known in the art. The background section of McIntire discusses use of poly(α-cyanoacrylates) and states that there is a need in the art for viscosity modifiers to be added to "the monomeric material [the α-cyanoacrylate]" (col. 1, lines 62-63). However, the teaching of a method of making a single viscosity modifier does not obviate the claimed invention. In the reference there is no teaching or suggestion of an adhesive composition comprising more than one cyanoacrylate monomer, nor combination with a plasticizer and an opacifying agent. Therefore, McIntire, taken in combination with the other cited references, does not teach or suggest the composition of the claimed invention.

Additionally, in Paper No. 10, Berger has been cited as teaching the use of two different monomers to provide enhanced flexibility of the polymer. However, it is respectfully submitted that Berger, taken in combination with the other cited references, does not teach all of the elements of the claimed invention. Berger does not teach addition of any two cyanoacrylate monomers to increase flexibility, but teaches specifically addition of a C_{10}-C_{12} alkyl cyanoacrylate ester to a C_1-C_8 alkyl cyanoacrylate ester to form a flexible cyanoacrylate polymer, which is preferably flexible enough not to need a plasticizer. The claimed invention, however, teaches use of the combination of monomers, preferably with different alkyl side chains, in order to modify the characteristics of the resulting polymer (for example, polymerization rate and/or flexibility) to what is optimal for a desired application (specification, page 16) and teaches the component in conjunction with a second component, containing a plasticizer. As Berger is directed to optimizing flexibility while minimizing plasticizer use, Berger teaches away from the claimed invention. One of skill in the art would not be motivated to combine the teachings of Berger with the other references to obtain the claimed invention.

It is respectfully submitted that not only do the cited references not teach all of the elements of the claimed invention, but there is also no motivation to combine these references for what they do teach.

The teaching or suggestion to make the claimed combination and the reasonable expectation of success must be both found in the prior art, and not based on applicant's disclosure. It is stated in section 2141.01 of the MPEP that a rejection of claims under 35 U.S.C §103 must be made without the benefit of hindsight afforded by the claimed invention. It is respectfully submitted that the present rejection for obviousness is based on improper hindsight. It is Applicants' assertion that one of skill in the art would not have selected the eleven cited references ranging from 1968 to 1997 from all the references regarding cyanoacrylates to assemble the claimed invention without the benefit of the teachings of the claimed invention. In this respect, one of skill in the art would not have had a reasonable expectation of success in the combination of two components, the first including at least two polymerizable alkyl cyanoacrylate monomers and the second including an oligomer of a polymerizable alkyl cyanoacrylate monomer, a plasticizer and an opacifying agent, where the composition would polymerize upon contact with an anionic environment. Accordingly, Applicants maintain that inventive steps were required, which would not have been obvious to those skilled in the art, to obtain the claimed composition and the methods of utilizing the same.

As the cited references do not suggest or motivate a combination of their teachings, one of skill in the art would not have reasonably expected the combination of references to produce a useful composition. Additionally, because all of the cited references, taken together do not teach or suggest all of the elements of the claimed invention, it is respectfully submitted that Evans in view of Tseng, Woodward, Clark, Hoffman, Krall, Almen, EP 0 747 069, Leung, McIntire and Berger does not anticipate the claimed invention under 35 U.S.C § 103(a). Withdrawal of the rejection is therefore respectfully requested.

CONCLUSION

In summary, for the reasons set forth herein, Applicants maintain that claims 1 and 4-53 clearly and patentably define the invention, respectfully request that the Examiner reconsider the various grounds set forth in the Office Action, and respectfully request the allowance of the claims which are now pending.

If the Examiner would like to discuss any of the issues raised in the Office Action, Applicant's representative, Lisa Haile, can be reached at (858) 677-1456 or the undersigned, at the number listed below. Please charge any additional fees, or make any credits, to Deposit Account No. 50-1355.

Respectfully submitted,

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COMPLETE LISTING OF THE CLAIMS

1. (Previously Amended) A composition comprising a first component and a second component, wherein said first component includes at least two polymerizable alkyl cyanoacrylate monomers, and wherein the second component includes an oligomer of a polymerizable alkyl cyanoacrylate monomer, a plasticizer, and an opacifying agent, wherein the composition polymerizes upon contact with an anionic environment.

2-3. (Cancelled)

4. (Previously Amended) The composition according to claim 1, wherein said alkyl cyanoacrylates of the first component are chosen such that the alkyl chain contains from 1 to 18 carbon atoms.

5. (Previously Amended) The composition according to claim 1, wherein said cyanoacrylates are selected from methyl cyanoacrylate, n-butyl cyanoacrylate, isobutyl cyanoacrylate, n-hexyl cyanoacrylate, 2-hexyl cyanoacrylate, n-octyl cyanoacrylate, or 2-ethylhexyl cyanoacrylate.

6. (Original) The composition according to claim 1, wherein said first component includes at least one polymerization inhibitor.

7. (Original) The composition according to claim 6, wherein said inhibitors act primarily to inhibit free radical polymerization.

8. (Original) The composition according to claim 7, wherein said inhibitors are present in the range of about 1 to 500 parts per million.

9. (Original) The composition according to claim 6, wherein at least one of said inhibitors acts primarily to inhibit anionic polymerization.

10. (Original) The composition according to claim 9, wherein said inhibitor is an acid.

11. (Original) The composition according to claim 10, wherein said acid is present in the range of about 50-500 parts per million.

12. (Original) The composition according to claim 11, wherein said acid is acetic acid or phosphoric acid.

13. (Original) The composition according to claim 12, wherein said acetic acid or phosphoric acid is present in the range of about 200 to 300 parts per million.

14. (Original) The composition according to claim 1, wherein said plasticizer is an esterified fatty acid.

15. (Previously Amended) The composition according to claim 14, wherein said esterified fatty acid is chosen from the group consisting of laurates, palmitates, oleates, myristates, or stearates.

16. (Original) The composition according to claim 15, wherein said esterified fatty acid is ethyl myristate.

17. (Previously Amended) The composition according to claim 1, wherein said opacifying agent is a metal.

18. (Original) The composition according to claim 17, wherein said metal is selected from gold, platinum, palladium, tantalum, titanium, or mixtures and alloys thereof.

19. (Original) The composition according to claim 18, wherein said metal is gold.

20. (Original) The composition according to claim 19, wherein said gold is in fine powder form with individual particles no larger than about 7 microns in diameter.

21. (Original) The composition according to claim 20, wherein said gold is in fine powder form with individual particles no larger than about 5 microns in diameter.

22. (Original) The composition according to claim 21, wherein said gold is in fine powder form with individual particles no larger than about 2 microns in diameter.

23. (Original) The composition according to claim 22, wherein said gold is in fine powder form with individual parties no larger than about 1 micron in diameter.

24. (Original) A composition comprising a first component and a second component, said first component comprising n-hexyl cyanoacrylate, methyl cyanoacrylate and phosphoric acid, said second component comprising an oligomer of n-hexyl cyanoacrylate, ethyl myristate, and gold, wherein said composition polymerizes upon contact with an anionic environment.

25. (Original) The composition according to claim 24, wherein said second component further includes a halogenated oil.

26. (Original) The composition according to claim 25, wherein said halogenated oil is iodinated castor oil.

27. (Previously Amended) A method of filling, occluding, partially filling, or partially occluding an unfilled volume or space in an anionic environment, said method comprising, administering a composition comprising a first component and a second component, wherein said first component includes at least two polymerizable alkyl cyanoacrylate monomers, and wherein said second component includes an oligomer of a polymerizable alkyl cyanoacrylate monomer, plasticizer, and an opacifying agent, wherein said composition polymerizes upon contact with said anionic environment when administered with a device comprising a means for stabilizing fluid flow distal or proximal to said space and a means for delivering said composition to said space, whereby said space is filled, occluded, partially filled, or partially occluded.

28. (Original) The methods according to claim 27, wherein and stabilizing means and delivering means are within one device.

29. (Original) The method according to claim 27, wherein said stabilizing means is in a first device, and said delivering means is in a second device.

30. (Original) The method according to claim 27, wherein said space is an existing space in human or animal body.

31. (Original) The method according to claim 30, wherein said existing space is created by a transiently placed external device.

32. (Original) The method according to claim 30, wherein said existing space is created by or resulting from a procedure.

33. (Original) The method according to claim 30, wherein said existing space is created by the placement or implantation of an object.

34. (Original) The method according to claim 30, wherein said existing space is created by the composition itself.

35. (Original) The method according to claim 30, wherein said existing space is a lumen of a passageway in the human body.

36. (Original) The method according to claim 30, wherein said existing space is a blood vessel.

37. (Original) The method according to claim 30, wherein said existing space is a duct.

38. (Original) A method for ablating diseased or undesired tissue, said method comprising administering a composition according to claim 1 to blood vessel(s) that feed said

tissue, whereby said blood vessel(s) are occluded, thereby cutting off blood supply to said tissue, whereby said diseased or undesired tissue is ablated.

39. (Original) The method according to claim 38, wherein said undesired tissue is an arteriovenous malformation.

40. (Original) The method according to claim 38, wherein said undesired tissue is a tumor.

41. (Original) The method according to claim 38, wherein said undesired tissue is an uterine leiomyoma.

42. (Original) A method for treating arteriovenous venous malformation (AVM) by cutting off the blood supply to said AVM, said method comprising administering a composition according to claim 1 to blood vessel(s) that feed said AVM, whereby said blood vessel(s) are occluded, thereby cutting off blood supply to said AVM, whereby said AVM is treated.

43. (Original) A method for treating a tumor by cutting off the blood supply to said tumor, said method comprising administering a composition according to claim 1 to blood vessel(s) that feed said tumor, whereby said blood vessel(s) are occluded, thereby cutting off blood supply to said tumor, whereby said tumor is treated.

44. (Original) A method for treating a uterine leiomyoma by cutting off the blood supply to said leiomyoma, said method comprising administering a composition according to claim 1 to blood vessel(s) that feed and leiomyoma, whereby said blood vessel(s) are occluded, thereby cutting off blood supply to said leiomyoma, whereby said uterine leiomyoma is treated.

45. (Original) A method for sterilizing a female mammal, said method comprising administering a composition according to claim 1 to the fallopian tubes of said female mammal

thereby preventing passage of eggs from the ovaries to the uterus of said female mammal, whereby said female mammal is sterilized.

46. (Previously Amended) A method of filling, occluding, partially filling, or partially occluding an unfilled volume or space in an anionic environment, said method comprising administering a composition comprising a first component and a second component, wherein said first component includes at least two polymerizable alkyl cyanoacrylate monomers, and wherein said second component includes an oligomer of a polymerizable alkyl cyanoacrylate monomer, a plasticizer, and an opacifying agent, wherein said composition polymerizes upon contact with said anionic environment when administered with a device comprising a temporary inflatable balloon and a catheter, whereby said space is filled, occluded, partially filled, or partially occluded.

47. (Original) A method for controlled delivery of a therapeutic, chemotherapeutic, or radiation delivery device, to a desired location in the human body, said method comprising combining said therapeutic, chemotherapeutic, or radiation delivery device with a composition according to claim 1, and delivering said combination to said desired location, whereby said therapeutic, chemotherapeutic, radiation delivery device, or gene therapy composition is gradually released at said desired location in the human body.

48. (Original) A method for delivering magnetic particles to a location in a mammalian body, said method comprising combining said magnetic particles with a composition according to claim 1, and delivering said combination to said location.

49. (Original) A method for adhering a first section of mammalian tissue to a second section of mammalian tissue, said method comprising contacting said first tissue with a composition according to claim 1, and contacting said second tissue with said first tissue, whereby said first tissue is adhered to said second tissue.

50. (Original) A method for adhering a section of mammalian tissue to a non-tissue surface, said method comprising contacting said tissue with a composition according to claim 1, and contacting said non-tissue surface with said section of mammalian tissue, whereby said tissue is adhered to said non-tissue surface.

51. (Original) The method according to claim 50, wherein said non-tissue surface is a medical device.

52. (Original) The method according to claim 51, wherein said medical device is a venous valve, a heart value, or a stent.

53. (Original) A method for delivering a composition according to claim 1 to a location in a mammalian body, said method comprising administering said composition with a device comprising a means for stabilizing fluid flow distal or proximal to said location, and a means for delivering said composition, whereby said composition is delivered to said location.